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Cross-coupling reaction of organobismuth dialkoxides with aryl bromides and iodides catalyzed by $Pd(PPh_3)_4$

Maddali L.N. Rao [a], Shigeru Shimada [a,*], Osamu Yamazaki [a], Masato Tanaka [a,b,*]

[a] National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba Central 5, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565, Japan
[b] Chemical Resources Laboratory, Tokyo Institute of Technology, 4259 Nagatsuda-cho, Midori-ku, Yokohama 226-8503, Japan

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Abstract

Cross-coupling reaction of organobismuth compounds bearing 2,6-pyridinedimethoxide ligands with aryl bromides and iodides was efficiently catalyzed by $Pd(PPh_3)_4$. Addition of two equivalents of Cs_2CO_3 or CsF improved the yields of the products, in particular for the reaction of aryl bromides. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Organobismuth compounds; Cross-coupling reaction; Palladium; Aryl halides

1. Introduction

Transition metal-catalyzed cross-coupling reaction of organometallic compounds with organic halides and triflates is one of the most important reactions to make C–C bonds, in particular for those containing sp^2- or sp-C atoms [1]. Various organometallic compounds such as organotin, boron, silicon, zinc, and magnesium compounds have been successfully utilized for the cross-coupling reactions.

On the other hand, organobismuth compounds are useful reagents for the transition metal-mediated or -catalyzed coupling reaction with various substrate [2]; for example, pentavalent and trivalent organobismuth compounds have been utilized for the Heck-type arylation of alkenes [3], arylation of alcohols and amines [4], cross-coupling reaction with acid chlorides [5], allyl halides [6] and terminal alkynes [7], homocoupling biaryl formation [5a,8], carbonylation reactions [9], and arylation of vinyl epoxides [10]. We have recently demonstrated that organobismuth compounds are also useful reagents for the cross-coupling reaction with aryl or alkenyl triflates and aryl halides: the reactions of organobismuth dialkoxides **1a**–**1d** with aryl- and alkenyl-triflates (Scheme 1) and the reactions of Ar_3Bi with aryl halides and triflates (Scheme 2) readily proceed to form the corresponding cross-coupled products in good yields [11,12].

The reaction of compounds **1** with aryl- and alkenyl-triflates proceeded in the presence of $Pd(PPh_3)_4$ without any additives. However, the reactivity of **1** to aryl bromides seemed to be much lower than that to triflates: the reaction of **1b** with 1-naphthyl triflate gave 80% of cross-coupled product while that of **1b** with 1-bromonaphthalene afforded only 15% of cross-coupled product [11]. We recently found that the addition of coordinating salt such as K_2CO_3 or CsF considerably improved the reactivity of Ar_3Bi toward aryl triflates, bromides, and iodides [12]. Here, we report the palladium-catalyzed cross-coupling reaction of **1a** and **1d** with aryl bromides and iodides and the influence of salt additives.

2. Results and discussion

2.1. Reaction of *1a* and *1d* with aryl bromides

Under the reaction conditions suitable for the cross-coupling reaction of **1a** with aryl triflates (10 mol% $Pd(PPh_3)_4$, 100 °C, 12 h in NMP (1-methyl-2-pyrrolidinone)) [11], the reaction of **1a** with 1-bromonaphtha-

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* Corresponding authors. Tel.: +81-298-61-4588; fax: +81-298-61-4511

E-mail address: s-shimada@aist.go.jp (S. Shimada).

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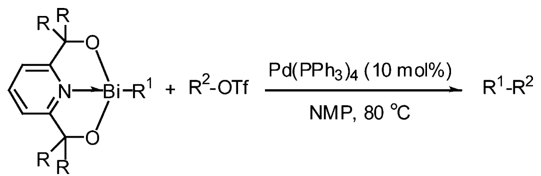
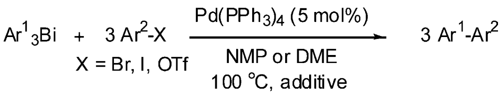


1a : R = Me, R^1 = Ph
1b : R = Et, R^1 = Ph
1c : R = ^{i}Pr, R^1 = Ph
1d : R = R^1 = Me

Scheme 1.



Scheme 2.

lene gave only 15% of cross-coupled product, 1-phenylnaphthalene, together with biphenyl (13%). However, the reactivity was dramatically enhanced by addition of Cs_2CO_3 (two equivalents to ArBr) to form the product in 88% yield. CsF (40%) and K_2CO_3 (32%) also showed slight improvement in the yield while NEt_3, LiCl, and KF were not effective.

The reaction of **1a** with electron-deficient aryl bromides, 4′-bromoacetophenone and 4-bromobenzonitrile, gave the cross-coupled products in moderate to good yields even in the absence of additives, while the yield became quantitative by the addition of Cs_2CO_3 (Table 1, entries 3–4 and 6–7) [13]. Other electron-deficient aryl bromides and 2-bromopyridine also gave phenylated products in excellent yields (Table 1, entries 9, 11–12, 14). On the other hand, as observed in the reaction of **1a**–**1d** with aryl triflates [11], an electron-rich aryl bromide, 4-bromotoluene, afforded the cross-coupled product only in a low yield even in the presence of Cs_2CO_3. (Table 1, entry 13). Methylation with **1d** (Table 1, entries 5, 8, 10) also proceeded albeit less efficiently than the phenylation with **1a**.

Table 1
Reaction of organobismuth dialkoxides **1a** and **1d** with aryl bromides [a]

$$\mathbf{1a}\text{ or }\mathbf{1d}+\text{Ar–Br}\xrightarrow[\text{NMP, 100 °C (additive, two equivalents)}]{\text{Pd(PPh}_3)_4\text{ (10 mol\%)}}\text{Ar–R}^1.$$

Entry	1a/1d	Ar	Additive	Yield (%) [b]
1 [c]	**1a**	1-Naphthyl	no	15
2	**1a**		Cs_2CO_3	88
3	**1a**	4-AcC_6H_4	no	63
4	**1a**		Cs_2CO_3	99
5	**1d**		Cs_2CO_3	69
6	**1a**	4-NCC_6H_4	no	79
7	**1a**		Cs_2CO_3	quant (95)
8	**1d**		Cs_2CO_3	52
9	**1a**	4-$PhCOC_6H_4$	Cs_2CO_3	96
10	**1d**		Cs_2CO_3	80
11	**1a**	3-AcC_6H_4	Cs_2CO_3	85
12	**1a**	3-$CF_3C_6H_4$	Cs_2CO_3	quant
13	**1a**	4-MeC_6H_4	Cs_2CO_3	36
14	**1a**	2-Pyridyl	Cs_2CO_3	99

[a] **1a** or **1d**:ArBr = 1.2:1.

[b] Yields were determined by GLC analysis of the crude reaction mixture by using hexadecane as an internal standard. Isolated yield is shown in parentheses.

[c] Reaction time, 12 h.

2.2. *Reaction of* **1a** *and* **1d** *with aryl iodides*

Aryl iodides, as expected, are more reactive than aryl bromides toward **1a** and **1d**. Phenylation of 1-iodonaphthalene with **1a** gave 1-phenylnaphthalene in a good yield in the absence of additives (Table 2, entry 1), and the yield became quantitative by the addition of two equivalents of Cs_2CO_3 (Table 2, entry 3) [13]. Electron-deficient aryl iodides afforded phenylated products in excellent yields even in the absence of additives (Table 2, entries 4, 6–7). It is noteworthy that even electron-rich aryl iodides gave phenylarenes in good yields when two equivalents of CsF or Cs_2CO_3 was added to the reaction system (Table 2, entries 9–10 and 12–13).

2.3. *Effects of salt additives*

The improvement of the yield by the addition of salts may be attributed to the formation of higher coordinated bismuth ‘ate’ complexes. The enhancement of the reactivity by coordinating additives is also known in the cross-coupling reaction of other organometallic compounds. For example, cross-coupling reaction of boronic acids or boronic esters requires base additives; anionic boronate intermediates seem to be the actual species which undergo the transmetalation [1b,1c]. Cross-coupling reaction of organosilicon compounds usually requires fluoride salts as activators; pentacoordinate fluorosilicates are the key intermediates in this reaction [14].

It is well known that bismuth often forms hypervalent compounds; organobismuth compounds can accommodate up to nine coordinations [15]. Unlike Ar_3Bi, compounds **1a**–**1d** already have intramolecular coordination by a nitrogen atom. However, their solid state structures have disclosed that they form dimers by the intermolecular coordination by the oxygen atom to the bismuth atom [16]. Although the formation of a stable ate complex from **1a** with Cs_2CO_3 was not observed [17], we presume that **1a**–**1d** can accommodate additional coordination of the salt promoters, which is likely to be associated with the reactivity enhancement of **1a** and **1d** in the cross-coupling reaction.

Table 2
Reaction of organobismuth dialkoxides **1a** and **1d** with aryl-iodides [a]

$$\mathbf{1a} \text{ or } \mathbf{1d} + \text{Ar–I} \xrightarrow[\text{NMP, 80 °C (additive, two equivalents)}]{\text{Pd(PPh}_3\text{)}_4\text{ (10 mol\%)}} \text{Ar–R}^1.$$

Entry	**1a/1d**	Ar	Time (h)	Additive	Yield (%) [b]
1	**1a**	1-Naphthyl	6	No	74
2	**1a**		6	CsF	86
3	**1a**		6	Cs_2CO_3	99(93)
4	**1a**	4-AcC_6H_4	3	No	96
5	**1d**		6	No	69
6	**1a**	4-AcC_6H_4	3	No	Quant
7	**1a**	3-$CF_3C_6H_4$	3	No	97
8	**1a**	4-MeC_6H_4	6	No	60
9	**1a**		6	CsF	85
10	**1a**		6	Cs_2CO_3	83(78)
11	**1a**	4-$MeOC_6H_4$	6	No	55
12	**1a**		6	CsF	61
13	**1a**		6	Cs_2CO_3	79
14	**1a**	2-Pyridyl	6	No	57
15	**1a**		6	Cs_2CO_3	93

[a] **1a** or **1d**:ArI = 1.2:1.

[b] Yields were determined by GLC analysis of the crude reaction mixture by using hexadecane as an internal standard. Isolated yields are shown in parentheses.

2.4. Reaction mechanism

Previously, we have proposed two possible catalytic cycles, cycle A and cycle B in Fig. 1, for the cross-coupling reaction of compounds **1** with aryl and alkenyl-triflates [11]. Cycle A is triggered by the oxidative addition of Bi–C bond to Pd(0), followed by the transmetalation with Ar–X and subsequent reductive elimination to give cross-coupled product and Pd(0) species. Cycle B is generally accepted as a mechanism for the cross-coupling reaction of organometallic compounds such as organoboron and organotin compounds: oxidative addition of Ar–X to Pd(0) species, a transmetalation step to form a diorganopalladium intermediate, and a subsequent reductive elimination step to form the cross-coupled product and the Pd(0) species [1].

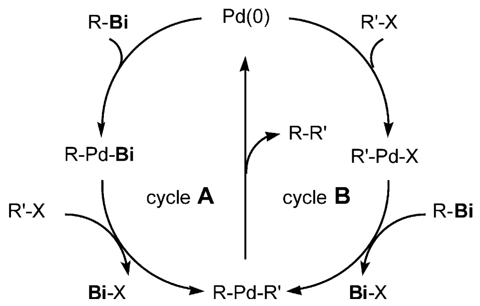


Fig. 1. Two possible catalytic cycles for the cross-coupling reaction of organobismuth compounds.

In the previous paper [11], we suggested that cycle A is more likely based mainly on the following information, (1) Bi–C bond is very weak [18]; (2) **1c** is more reactive than 4-acetylphenyl triflate in oxidative addition reaction to $Pt(PEt_3)_4$ [19].

However, further study supported cycle B rather than cycle A, (1) oxidative addition of **1a** toward $Pd(PPh_3)_4$ was not observed by NMR. Instead, gradual decomposition of $Pd(PPh_3)_4$ took place when the mixture of $Pd(PPh_3)_4$ and **1a** in $(CD_3)_2NCDO$ was heated at 100 °C; (2) electron deficient aryl halides gave better yields of cross-coupled products than electron rich aryl halides; this observation is compatible with the oxidative addition step of cycle B; (3a) the improvement of the yields by salt additives and (3b) higher reactivity of $(p\text{-}MeC_6H_4)_3Bi$ or Ph_3Bi than $(p\text{-}FC_6H_4)_3Bi$ in the cross-coupling reaction with 1-bromonaphthalene [12] suggest that electron-rich organobismuth species have higher reactivity probably because they have higher ability to transfer aryl-group in the transmetalation step of cycle B; (4) [*trans*-Pd(Br)(p-NCC_6H_4)$(PPh_3)_2$], an intermediate in cycle B, reacted with **1a** at 100 °C in NMP for 6 h to produce the cross-coupled product, 4-biphenylcarbonitrile, in 84% yield. Based on these results, it is likely that the cross-coupling reaction of **1a**–**d** and Ar_3Bi with organic triflates and aryl halides proceeds through cycle B. The oxidative addition step and the transmetalation step are probably comparable in their reaction rate and either of them is rate-determining depending on substrates and reaction conditions. If the reactivity of aryl halides or bismuth compounds is low, decomposition of the catalyst becomes competitive to the cross-coupling reaction and the yield of the cross-coupled product decreases.

3. Experimental

3.1. General

All manipulations of air-sensitive materials were carried out under a nitrogen atmosphere using standard Schlenk tube techniques. Anhydrous NMP was purchased from Kanto Chemicals and degassed before use. Compounds **1a** and **1d** were prepared as described previously [16]. [*Trans*-Pd(Br)(p-NCC_6H_4)$(PPh_3)_2$] [20] was prepared as described in the literature for the preparation of [*trans*-Pd(Cl)(p-NCC_6H_4)$(PPh_3)_2$] [21].

3.2. Reaction of 1a and 1d with aryl halides

3.2.1. Typical reaction procedure

A mixture of **1a** (144 mg, 0.30 mmol), 4-bromobenzonitrile (46 mg, 0.25 mmol), Cs_2CO_3 (163 mg, 0.50 mmol), and $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) in 3 ml of NMP was heated at 100 °C for 6 h under N_2. After the addition of hexadecane (internal standard), the mixture was analyzed by GC to determine the yield of 4-biphenylcarbonitrile (100%). Biphenyl was not detected by GC analysis. The crude mixture was dissolved in EtOAc (90 ml) and washed with water (10 ml), 10% aqueous (aq.) HCl (10 ml), water (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by preparative TLC (hexane–EtOAc = 5/1) to give 43 mg (95%) of 4-biphenylcarbonitrile.

3.3. *Reaction of [trans-Pd(Br)(p-NCC$_6$H$_4$)(PPh$_3$)$_2$] with* ***1a***

A mixture of **1a** (72 mg, 0.15 mmol), [*trans*-Pd(Br)(*p*-NCC_6H_4)(PPh_3)$_2$] (102 mg, 0.125 mmol), and PPh_3 (65 mg, 0.25 mmol) in 1.5 ml of NMP was heated at 100 °C for 6 h under N_2. The crude mixture was dissolved in EtOAc (45 ml) and washed with water (10 ml), 10% aq. HCl (10 ml), water (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by preparative TLC (hexane–EtOAc = 5/1) to give 19.0 mg (84%) of 4-biphenylcarbonitrile.

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References

[1] (a) F. Diederich, P.J. Stang (Eds.), Metal-Catalyzed Cross-Coupling Reactions, Wiley-VCH, 1998;
(b) A. Suzuki, J. Organomet. Chem. 576 (1999) 147;
(c) N. Miyaura, Topp. Curr. Chem. 219 (2002) 11;
(d) T. Hiyama, E. Shirakawa, Topp. Curr. Chem. 219 (2002) 61;
(e) K. Fugami, M. Kosugi, Topp. Curr. Chem. 219 (2002) 87;
(f) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, Chem. Rev. 102 (2002) 1359.

[2] (a) H. Suzuki, T. Ikegami, Y. Matano, Synthesis (1997) 249;
(b) H. Suzuki, Y. Matano, in: N.C. Norman (Ed.), Chemistry of Arsenic, Antimony and Bismuth (Chapter 6), Blackie Academic and Professional, 1998;
(c) M. Wada, N. Miyoshi, J. Syn. Org. Chem. Jpn. 57 (1999) 689;
(d) M. Wada, N. Miyoshi, Chem. Abstr. 131 (1999) 169911g;
(e) G.I. Elliott, J.P. Konopelski, Tetrahedron 57 (2001) 5683;
(f) H. Suzuki, Y. Matano (Eds.), Organobismuth Chemistry, Elsevier, 2001;
(g) Y. Matano, J. Syn. Org. Chem. Jpn. 59 (2001) 834;
(h) Y. Matano, Chem. Abstr. 135 (2001) 371248j.

[3] (a) R. Asano, I. Moritani, Y. Fujiwara, S. Teranishi, Bull. Chem. Soc. Jpn. 46 (1973) 2910;
(b) T. Kawamura, K. Kikukawa, M. Takagi, T. Matsuda, Bull. Chem. Soc. Jpn. 50 (1977) 2021.

[4] (a) V.A. Dodonov, A.V. Gushchin, T.G. Brilkina, Zh. Obshch. Khim. 55 (1985) 2514;
(b) V.A. Dodonov, A.V. Gushchin, T.G. Brilkina, J. Gen. Chem. USSR (English Translation) 55 (1985) 2232;
(c) D.H.R. Barton, J.P. Finet, J. Khamsi, Tetrahedron Lett. 27 (1986) 3615;
(d) D.H.R. Barton, J.P. Finet, J. Khamsi, Tetrahedron Lett. 27 (1986) 3619;
(e) D.M.T. Chan, Tetrahedron Lett. 37 (1996) 9013.

[5] (a) D.H.R. Barton, N. Ozbalik, M. Ramesh, Tetrahedron 44 (1988) 5661;
(b) H. Suzuki, T. Murafuji, N. Azuma, J. Chem. Soc. Perkin Trans. 1 (1992) 1593.

[6] (a) M. Wada, H. Ohki, J. Synth. Org. Chem. Jpn. 47 (1989) 425;
(b) M. Wada, H. Ohki, Chem. Abstr. 111 (1989) 38573n;
(c) X. Huang, J.L. Wu, Chin. Chem. Lett. 8 (1997) 759;
(d) X. Huang, J.L. Wu, Chem. Abstr. 127 (1997) 358654d.

[7] S.A. Lermontov, I.M. Rakov, N.S. Zefirov, P.J. Stang, Tetrahedron Lett. 37 (1996) 4051.

[8] T. Ohe, T. Tanaka, M. Kuroda, C.S. Cho, K. Ohe, S. Uemura, Bull. Chem. Soc. Jpn. 72 (1999) 1851.

[9] (a) C.S. Cho, T. Ohe, O. Itoh, S. Uemura, J. Chem. Soc. Chem. Commun. (1992) 453;
(b) C.S. Cho, Y. Yoshimori, S. Uemura, Bull. Chem. Soc. Jpn. 68 (1995) 950.

[10] S.K. Kang, H.C. Ryu, Y.T. Hong, M.S. Kim, S.W. Lee, J.H. Jung, Synth. Commun. 31 (2001) 2365.

[11] M.L.N. Rao, S. Shimada, M. Tanaka, Org. Lett. 1 (1999) 1271.

[12] M.L.N. Rao, O. Yamazaki, S. Shimada, T. Tanaka, Y. Suzuki, M. Tanaka, Org. Lett. 3 (2001) 4103.

[13] In the reaction of **1a**, biphenyl was occasionally produced as a by-product in 10–40% yields based on **1a**.

[14] (a) Y. Hatanaka, K. Goda, Y. Okahara, T. Hiyama, Tetrahedron 50 (1994) 8301;
(b) T. Hiyama, in: F. Diederich, P.J. Stang (Eds.), Metal-Catalyzed Cross-Coupling Reactions (Chapter 10), Wiley-VCH, 1998.

[15] T. Ogawa, in: H. Suzuki, Y. Matano (Eds.), Organobismuth Chemistry (Chapter 6), Elsevier, 2001.

[16] S. Shimada, M.L.N. Rao, M. Tanaka, Organometallics 19 (2000) 931.

[17] Most of Cs_2CO_3 seemed not to dissolve in $(CD_3)_2NCDO$ in an attempted reaction of **1a** with Cs_2CO_3 (**1a**:Cs_2CO_3 = 2:1). ^1H-NMR spectrum of this mixture did not show any new signal, but slight chemical shift changes (up to 0.016 ppm) were observed for some of signals of **1a**. The latter observation may be attributable to a formation of a small amount of an ate complex that is in equilibrium with **1a**.

[18] Mean bond-dissociation energy of Bi–Ph bond of Ph_3Bi was estimated to be 193.9 ± 10.8 kJ mol^{-1}. W.V. Steele, J. Chem. Thermodyn. 11 (1979) 187.

[19] S. Shimada, M. Tanaka, unpublished results.

[20] (a) C. Amatore, A. Jutand, F. Khalil, M.F. Nielsen, J. Am. Chem. Soc. 114 (1992) 7076;
(b) P. Fitton, E.A. Rick, J. Organomet. Chem. 28 (1971) 287.

[21] W.A. Herrmann, C. Broßmer, T. Priermeier, K. Öfele, J. Organomet. Chem. 481 (1994) 97.